CHAPTER ONE

General introduction and outline of the thesis
GENERAL INTRODUCTION

Malnutrition during hospitalisation leads to an increased morbidity, mortality, length of hospital stay, and is associated with higher costs (1). It is essential to optimise nutritional support for surgical patients by the provision of adequate amounts of energy and proteins to prevent catabolism, diminish the suppression of immune competence, and decrease septic complications (2). Therefore, the objective of this thesis was to gain insight in perioperative conditions and how these can be optimised by nutritional interventions. Accordingly, the Enhanced Recovery of patients After Surgery (ERAS) guidelines have become an important focus of perioperative nutritional management, to minimise the complications associated with malnutrition (3). These guidelines are intended to give evidence-based recommendations for the use of nutritional support in the surgical patient. Not only surgery influences the response to nutritional support, many of the perioperative routines also have a major impact on how the different nutritional treatments are tolerated by patients postoperatively.

Surgery, like any injury to the body, elicits a series of reactions including the release of stress hormones and inflammatory mediators. The release of these mediators to the circulation has a major impact on the metabolism of the human body. These mediators are involved in the breakdown of glycogen, fat, and protein stores by the release of glucose, free fatty acids and amino acids into the circulation. These metabolic changes are important for diverting these essential substrates from non-essential tasks to more important functions such as healing and immune response (4). These metabolic changes result in sustained protein catabolism, leading to a negative nitrogen balance and to muscle degradation and wasting (5). Reducing the
stress of surgery can minimize catabolism, support anabolism throughout surgical treatment, and allow patients to recover substantially better and faster. The ERAS program involves a series of components that combine the aim to minimize stress and to facilitate the return of physical function. This includes preoperative preparation and medication, fluid balance, anaesthesia and postoperative analgesia, pre- and postoperative nutrition, and mobilization (6). The so-called ‘fast track’ program for colorectal surgery particularly, implements the ERAS guidelines and has been successful in promoting rapid recovery and shortening the length of hospital stay.

The success of these programs depends on a multi factorial approach. Several components, which are part of ERAS, are elucidated in this thesis. New insights and suggestions for optimization of existing guidelines will improve perioperative strategies in the surgical patient.

**OUTLINE OF THE THESIS**

The composition of enteral nutrition and how this may influence the digestion and absorption of nutrients is described in PART I. An introduction for PART I can be found in CHAPTER 2.

There are various ways to feed surgical patients, including enteral and parenteral nutrition. Enteral nutrition is the preferred route of feeding over parenteral nutrition for the critically ill patient requiring nutritional support (7). Compared to enteral nutrition, parenteral nutrition is associated with increased infectious complications and an increased mortality (8). By contrast, enteral nutrition can preserve the intestinal integrity and can play a major role in the prevention of mucosal atrophy and bacterial translocation (9). Enteral nutrition is usually well tolerated; however, the solidification of enteral nutrition by coagulation can cause gastrointestinal obstruction. Solidification of enteral nutrition can lead to serious complications such as small bowel obstruction, mural abscesses, haemorrhages, ulcers, pancreatitis, small bowel necrosis, bowel perforation and even death (10). In CHAPTER 3 all literature on the solidification of enteral nutrition is reviewed, to identify the predisposing factors for developing this severe complication and to discuss the underlying mechanism. Critically ill patients may have potential risk factors for solidification of enteral nutrition. Awareness of these risk factors will help intensive care specialists take appropriate actions to prevent the solidification of enteral nutrition.

It has been suggested that enteral nutrition containing insoluble fibers plays a role in the solidification and cases of bowel obstruction have been reported in literature. For that reason, the guidelines of the American Society of Parenteral and Enteral Nutrition (ASPEN) recommend avoiding the administration of insoluble fibers in critically ill patients (7). This statement is based on two articles reporting 5 cases, without considering other possible factors (11, 12). To clarify the effect of insoluble fibers on the solidification of enteral nutrition, this thesis includes an in vitro study using an artificial gastrointestinal model developed by TNO (Netherlands Organization for Applied Scientific Research) in collaboration with Nutricia Research. In CHAPTER 4 the findings are described on how increasing concentrations of soluble fibers (acacia fiber, oligofructose and inulin) and insoluble fibers (soy polysaccharide, resistant starch and alpha cellulose) affect the solidification of a standard 100% casein based enteral nutrition in an artificial gastric digestion model. Previous in vitro studies show that
casein protein is the major contributor to the coagulation of enteral nutrition. Coagulation can be prevented by adding non-coagulating protein to the enteral nutrition, e.g. soy, pea and whey protein (13).

There are several medical conditions that require feeding via an enteral tube placed in the small intestine. These include a high risk for aspiration or intolerance to gastric feeding. In CHAPTER 5 the impact of the administration of casein on protein digestion and amino acid absorption is studied. This study is the first to compare in vivo dietary protein digestion and absorption kinetics following jejunal versus gastric casein feeding in healthy young males. To allow the in vivo assessment of dietary protein digestion and absorption kinetics intrinsically L-[1-13C] phenylalanine-labeled casein protein was applied that was produced by collecting milk protein from lactating cows that were infused with large amounts of L-[1-13C]phenylalanine (14).

PART II provides more insights in the effect of food intake on the endocrine response in the gut. An introduction for PART II can be found in CHAPTER 6. Literature on the therapeutic role of gastrointestinal hormones in the treatment of delayed gastric emptying is reviewed in CHAPTER 7. Delayed gastric emptying occurs in approximately 50% of the mechanically ventilated critically ill patients, and it prevents an effective delivery of enteral nutrition (15). Therefore, it is a major goal for intensive care specialists to treat delayed gastric emptying to allow early enteral feeding. Currently available prokinetics have limitations in terms of sustained efficacy and side-effects. We summarize the mechanisms of action and discuss the possible utility of gastrointestinal hormones to prevent or treat delayed gastric emptying in critically ill patients. Moreover, this chapter also gives more clarity on the function and dysfunction of gastrointestinal hormones in critically ill patients. Patients with delayed gastric emptying or high gastric residuals are candidates for jejunal feeding. The impact of gastric versus jejunal feeding on circulating plasma glucose and amino acid concentrations and the associated endocrine response remains largely unexplored. In CHAPTER 8 the impact of administrating enteral nutrition either gastric or jejunal is investigated on endocrine responses (PYY, CCK, Ghrelin, GLP-1, and GLP-2), and digestion and absorption of macronutrients in vivo in healthy young males.

One of the key aspects of the ERAS guidelines is to re-establish oral feeding as early as possible after surgery. Whereas early enteral feeding improves GI motility, decreases infectious complication, length of hospital stay, and intensive care unit mortality (16). Early enteral nutrition can only be achieved when the condition of the patients allows this. This is reflected by the function of the enterocyte in the small intestine. A functional enterocyte is needed for maintaining or improving the nutritional status and ensuring an intact barrier function to prevent bacterial translocation. Enterocyte dysfunction is far more common than previously assumed in critically ill patients. In CHAPTER 9 an intestinal ischaemia reperfusion animal model was used to investigate whether preoperative carbohydrate loading increases spontaneous postoperative food intake, intestinal barrier function and the catabolic response.

In CHAPTER 10 conclusions from the previous chapters are placed in a broader perspective. Finally, we provide recommendations for future studies.
REFERENCES